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10/540,390	01/03/2006	Jonathan Baell	21415-0019	3533

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EXAMINER	
HA, JULIE	
ART UNIT	**PAPER NUMBER**
1654	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/540,390	BAELL, JONATHAN	
	Examiner	Art Unit	
	Julie Ha	1654	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 1 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 1-48 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) _____ is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) 1-48 are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

1. Restriction is required under 35 U.S.C. 121 and 372.

This application contains the following inventions or groups of inventions which are not so linked as to form a single general inventive concept under PCT Rule 13.1.

In accordance with 37 CFR 1.499, applicant is required, in reply to this action, to elect a single invention to which the claims must be restricted.

Group 1, claim(s) 32 and 41, drawn to a conformationally constrained compound or pharmaceutically acceptable salt or prodrug thereof having SEQ ID NO:4.

Group 2, claim(s) 32 and 41, drawn to a conformationally constrained compound or pharmaceutically acceptable salt or prodrug thereof having SEQ ID NO:5.

Group 3, claim(s) 32 and 41, drawn to a conformationally constrained compound or pharmaceutically acceptable salt or prodrug thereof having SEQ ID NO:6.

Group 4, claim(s) 32 and 41, drawn to a conformationally constrained compound or pharmaceutically acceptable salt or prodrug thereof having SEQ ID NO:7.

Group 5, claim(s) 32 and 41, drawn to a conformationally constrained compound or pharmaceutically acceptable salt or prodrug thereof having SEQ ID NO:8.

Group 6, claim(s) 32 and 41, drawn to a conformationally constrained compound or pharmaceutically acceptable salt or prodrug thereof having SEQ ID NO:9.

Group 7, claim(s) 32 and 41, drawn to a conformationally constrained compound or pharmaceutically acceptable salt or prodrug thereof having SEQ ID NO:10.

Group 8, claim(s) 32 and 41, drawn to a conformationally constrained compound or pharmaceutically acceptable salt or prodrug thereof having SEQ ID NO:11.

Group 9, claim(s) 32 and 41, drawn to a conformationally constrained compound or pharmaceutically acceptable salt or prodrug thereof having SEQ ID NO:12.

Group 10, claim(s) 32 and 41, drawn to a conformationally constrained compound or pharmaceutically acceptable salt or prodrug thereof having SEQ ID NO:13.

Group 11, claim(s) 32 and 41, drawn to a conformationally constrained compound or pharmaceutically acceptable salt or prodrug thereof having SEQ ID NO:14.

Group 12, claim(s) 42, drawn to a an assay for identifying compounds which bind to a member of the Bcl-2 family of proteins, the assay comprising the steps of: (a) providing a candidate compound to be tested; (b) containing a Bcl-2 family protein with the candidate compound and a peptide comprising SEQ ID NO:37; (c) determining whether the candidate compound has bound to the Bcl-2 family protein.

Group 13, claim(s) 43, drawn to a an assay for identifying compounds which bind to a member of the Bcl-2 family of proteins, the assay comprising the steps of: (a) providing a candidate compound to be tested; (b) containing a Bcl-2 family protein with the candidate compound and a peptide comprising SEQ ID NO:38; (c) determining whether the candidate compound has bound to the Bcl-2 family protein.

Group 14, claim(s) 44, drawn to a method of regulating the death of a cell, comprising contacting the cell with an effective amount of a conformationally constrained compound, or a pharmaceutically acceptable salt or prodrug thereof, the compound comprising SEQ ID NO:1.

Group 15, claim(s) 44, drawn to a method of regulating the death of a cell, comprising contacting the cell with an effective amount of a conformationally constrained compound, or a pharmaceutically acceptable salt or prodrug thereof, the compound comprising SEQ ID NO:2.

Group 16, claim(s) 44, drawn to a method of regulating the death of a cell, comprising contacting the cell with an effective amount of a conformationally constrained compound, or a pharmaceutically acceptable salt or prodrug thereof, the compound comprising SEQ ID NO:3.

Group 17, claim(s) 45, drawn to a method of inducing apoptosis in unwanted or damaged cells, comprising contacting the damaged or unwanted cells with an effective amount of a conformationally constrained compound, or a pharmaceutically acceptable salt or prodrug thereof, the compound comprising SEQ ID NO:1.

Group 18, claim(s) 45, drawn to a method of inducing apoptosis in unwanted or damaged cells, comprising contacting the damaged or unwanted cells with an effective amount of a conformationally constrained compound, or a pharmaceutically acceptable salt or prodrug thereof, the compound comprising SEQ ID NO:2.

Group 19, claim(s) 45, drawn to a method of inducing apoptosis in unwanted or damaged cells, comprising contacting the damaged or unwanted cells with an effective amount of a conformationally constrained compound, or a pharmaceutically acceptable salt or prodrug thereof, the compound comprising SEQ ID NO:3.

Group 20, claim(s) 46-48, drawn to a method of treatment and/or prophylaxis of a pro-survival Bcl-2 family member-mediated disease or condition, in a mammal, comprising administering to the mammal an effective amount of a conformationally constrained compound, or a pharmaceutically acceptable salt or prodrug thereof, the compound comprising SEQ ID NO: 1.

Group 21, claim(s) 46-48, drawn to a method of treatment and/or prophylaxis of a pro-survival Bcl-2 family member-mediated disease or condition, in a mammal, comprising administering to the mammal an effective amount of a conformationally constrained compound, or a pharmaceutically acceptable salt or prodrug thereof, the compound comprising SEQ ID NO: 2.

Group 22, claim(s) 46-48, drawn to a method of treatment and/or prophylaxis of a pro-survival Bcl-2 family member-mediated disease or condition, in a mammal, comprising administering to the mammal an effective amount of a conformationally constrained compound, or a pharmaceutically acceptable salt or prodrug thereof, the compound comprising SEQ ID NO: 3.

Linking Claims

2. Claims 1-32 and 34-40 link(s) inventions 1 through 11. The restriction requirement among the linked inventions is **subject to** the nonallowance of the linking claim(s), claims 1-32 and 34-40. Upon the indication of allowability of the linking claim(s), the restriction requirement as to the linked inventions **shall** be withdrawn and any claim(s) depending from or otherwise requiring all the limitations of the allowable linking claim(s) will be rejoined and fully examined for patentability in accordance with 37 CFR 1.104 **Claims that require all the limitations of an allowable linking claim** will be entered as a matter of right if the amendment is presented prior to final rejection or allowance, whichever is earlier. Amendments submitted after final rejection are

governed by 37 CFR 1.116; amendments submitted after allowance are governed by 37 CFR 1.312.

3. Applicant(s) are advised that if any claim presented in a continuation or divisional application is anticipated by, or includes all the limitations of, the allowable linking claim, such claim may be subject to provisional statutory and/or nonstatutory double patenting rejections over the claims of the instant application. Where a restriction requirement is withdrawn, the provisions of 35 U.S.C. 121 are no longer applicable. *In re Ziegler*, 443 F.2d 1211, 1215, 170 USPQ 129, 131-32 (CCPA 1971). See also MPEP § 804.01.

4. The inventions listed as Groups 1-22 do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons: The peptide sequence of the conformationally constrained compounds or a pharmaceutical salt do not share a core structural feature, and the peptide sequences are patentably independent and distinct. The peptide sequences are different and therefore, each sequence is structurally distinct. There is no common structure present. For example, peptide sequence of SEQ ID NO:4 has the sequence Xaa (variable amino acid and its side chain is linked to position 8 by a linker)-Xaa (hydrophobic)-Xaa (small amino acid)-Xaa (variable amino acid)-Xaa (variable amino acid)-Xaa (hydrophobic)-Xaa (variable amino acid)-Xaa (variable amino acid and its side chain is linked to position 1 by a linker)-Xaa (hydrophobic); peptide sequence of SEQ ID NO: 5 has the sequence Xaa (variable amino acid and its side chain is linked to position 8 by a linker)-Xaa (hydrophobic)-Xaa (small amino acid)-Xaa (variable amino acid)-Xaa (variable amino acid)-Xaa (hydrophobic)-Xaa (variable amino acid)-Xaa (variable amino acid and its side chain is linked to position 1 by a linker)-Xaa (hydrophobic)-Xaa (small amino acid)-Xaa (negatively charged amino acid)-Xaa (variable amino acid)-Xaa (hydrophobic). Since there are many different possible hydrophobic amino acids, and many different possibilities of variable amino acids, there is no core structure of the conformationally constrained compound.

5. The situation involving the so-called Markush practice wherein a single claim defines alternatives (chemical or non-chemical) is also governed by PCT Rule 13.2. In this special situation, the requirement of a technical interrelationship and the same or corresponding special technical features as defined in PCT Rule 13.2, shall be considered to be met when the alternatives are of a similar nature.

6. When the Markush grouping is for alternatives of chemical compounds, they shall be regarded as being of a similar nature where the following criteria are fulfilled:

(A) All alternatives have a common property or activity; and
(B)
(1) A common structure is present, i.e., a significant structural element is shared by all of the alternatives; or
(B)
(2) In cases where the common structure cannot be the unifying criteria, all alternatives belong to a recognized class of chemical compounds in the art to which the invention pertains.

7. In paragraph (B)(1), above, the words "significant structural element is shared by all of the alternatives" refer to cases where the compounds share a common chemical structure which occupies a large portion of their structures, or in case the compounds have in common only a small portion of their structures, the commonly shared structure constitutes a structurally distinctive portion in view of existing prior art, and the common structure is essential to the common property or activity. The structural element may be a single component or a combination of individual components linked together.

8. In paragraph (B)(2), above, the words "recognized class of chemical compounds" mean that there is an expectation from the knowledge in the art that members of the class will behave in the same way in the context of the claimed invention. In other words, each member could be substituted one for the other, with the expectation that the same intended result would be achieved.

Election of Species

9. This application contains claims directed to more than one species of the generic invention. These species are deemed to lack unity of invention because they are not so linked as to form a single general inventive concept under PCT Rule 13.1.

The species are as follows:

Different amino acid sequences: for example, SEQ ID NOS: 1-3 (species within these sequences) and 15-36;

Different variables associated with the different amino acid sequences: R, R', Zaa_1 and Zaa_2, m, n, linker (L);

Different Bcl-2 family protein;

Different species of diseases and conditions: inflammatory condition, cancer or an autoimmune disorder.

10. Applicant is required, in reply to this action, to elect a single species to which the claims shall be restricted if no generic claim is finally held to be allowable. The reply must also identify the claims readable on the elected species, including any claims subsequently added. An argument that a claim is allowable or that all claims are generic is considered non-responsive unless accompanied by an election.

11. If one of the groups from Groups 1-11 is elected, the Applicant is required to elect a single disclosed species of conformationally constrained compound (i.e., peptide sequence (amino acid identified) and all of the variables identified to encompass all of the variables to arrive at a single conformationally constrained compound). For example, Applicant elects Group 1 and elects SEQ ID NO:17 as species. If one of the groups from 12 or 13, Applicant is required to elect a single disclosed Bcl-2 family peptide, a candidate compound. For example, Applicant elects Group 13 and elects Bcl-XL and a candidate compound of SEQ ID NO: 17. If one of the groups from Groups 14-22 is elected, Applicant is required to elect a single disclosed species within the genus compound having an amino acid sequence (I) (SEQ ID NO: 1, 2 or 3) that would encompass all of the variables to arrive at a single disclosed compound species. For example, Applicant elect Group 14 and having SEQ ID NO:1 wherein R is an acyl, amino acid residue 1 is F, amino acid residues 2 and 3 are W and R respectively, amino acid residue 4 is L, amino acid residue 5 is G, amino acid residue 6 is D, amino acid residue 7 is N, and amino acid residue 8 is V and the linker is $-NH(CH_2)_4NH-$. This

species is wherein n is 0 and m is 1, and R' is NH_2. Additionally, if one of groups from Groups 20-22 is elected, Applicant is required to further elect a single disclosed species of the disease or condition for treatment. The disease or condition elected should be a subspecies within the genus, since the subspecies are patentably independent and distinct. For example, Applicant elects breast cancer as the disease for treatment. Please note that the examples provided are only for exemplary purposes. Applicant can elect any species that is disclosed.

12. Upon the allowance of a generic claim, applicant will be entitled to consideration of claims to additional species which are written in dependent form or otherwise include all the limitations of an allowed generic claim as provided by 37 CFR 1.141. If claims are added after the election, applicant must indicate which are readable upon the elected species. MPEP § 809.02(a).

13. The claims are deemed to correspond to the species listed above in the following manner:

3-6, 8, 10-11, 17-31 and 34-40.

The following claim(s) are generic: 1-2, 7, 9, 12-16, 32-33 and 41-48.

14. The species listed above do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, the species lack the same or corresponding special technical features for the following reasons: Different amino acid sequences having different variables are patentably independent and distinct due to the amino acid content leading to different structures. For example, since the SEQ ID NOS: 1-14 comprise variable amino acid content and other variables R, R', m, n and so forth, each peptide sequences have patentably different structure. This would lead to individual searches. For example, within SEQ ID NO:1, there are many different peptide sequences since SEQ ID NO:1 is Xaa (hydrophobic)-Xaa (variable amino acid)-Xaa (variable amino acid)-Xaa (hydrophobic)-Xaa (small amino acid)-Xaa (negatively charged amino acid)-Xaa (variable amino acid)-Xaa (hydrophobic). Since there are 20 naturally occurring amino acids as well as non-natural amino acids such as D-isomers,

there are innumerable numbers of possibilities for SEQ ID NO:1. Additionally, there are different hydrophobic amino acids, variable amino acids, and negatively charged amino acids. Thus, the possible peptide sequence of SEQ ID NO:1 is vast. Same analysis is applied to SEQ ID NOS: 2-14. Furthermore, for example, SEQ ID NO:17 (Ac-IAQ-Zaa_1-LRRIGD-Zaa_2-F-NH_2, wherein there is a linker between Zaa_1 and Zaa_2) is patentably independent and distinct from SEQ ID NO:22 (Ac-VGR-Zaa_1-LAIIGD-Zaa_2-M-NH_2, wherein there is a linker between Zaa_1 and Zaa_2). Furthermore, for example, even within SEQ ID NO:17, there are different possibilities, due to different Zaa_1, Zaa_2, and linkers. Due to the structural differences between the compounds, each compound would have to be searched separately. There is no common core structure. Different Bcl-2 family proteins are patentably independent and distinct due to structural differences between the proteins. This would require independent searches. Further, search for one would not necessarily lead to the other. Different diseases and conditions are patentably independent and distinct because of different mechanisms and cells that are involved. For example, inflammatory condition may include arthritis for example, and these are patentably independent and distinct from cancer. Arthritis is inflammation of joints, while cancer is a malignant and invasive growth or tumor (dictionary definition). Within these conditions and diseases, there are subspecies, because of the different cells that are involved. For example, different types of cancers are patentably independent and distinct because the cells involved are patentably independent and distinct. Breast cancer is not the same as lung cancer, since breast cancer involves the granular tissue of the breast while lung cancer involves the epithelial cells of the lung. Further, search for one would not necessarily lead to the other.

15. Applicant is advised that the reply to this requirement to be complete must include (i) an election of a species or invention to be examined even though the requirement be traversed (37 CFR 1.143) and (ii) identification of the claims encompassing the elected invention.

16. The election of an invention or species may be made with or without traverse. To reserve a right to petition, the election must be made with traverse. If the reply does not distinctly and specifically point out supposed errors in the restriction requirement, the election shall be treated as an election without traverse.

17. **Should applicant traverse on the ground that the inventions or species are not patentably distinct, applicant should submit evidence or identify such evidence now of record showing the inventions or species to be obvious variants or clearly admit on the record that this is the case. In either instance, if the examiner finds one of the inventions unpatentable over the prior art, the evidence or admission may be used in a rejection under 35 U.S.C.103(a) of the other invention.**

Conclusion

18. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Julie Ha whose telephone number is 571-272-5982. The examiner can normally be reached on Mon-Fri, 8:00 am to 4:30 pm.

19. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Cecilia Tsang can be reached on 571-272-0562. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

20. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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12/6/07
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PRIMARY EXAMINER